REMARKS

Claim 18 is pending in the application. Claim 18 has been amended. Support for the amendment can be found in the specification at, e.g., page 27, lines 23-26. No new matter has been added.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 2-4 of the Office Action, claim 18 was rejected as failing to comply with the written description requirement. According to the Office Action, "Applicant is not in possession of the claimed method, because Applicant is not in possession of the generically recited 'AILIM.'"

Claim 18 has been amended to recite the term "human AILIM." It is applicants' understanding, in view of the remarks at page 4 of the Office Action, that this amendment overcomes the rejection of claim 18. Accordingly, applicants respectfully request that the Examiner withdraw the written description rejection of claim 18.

35 U.S.C. §103(a) (Obviousness)

At pages 5-6 of the Office Action, claim 18 was rejected as unpatentable over Kroczek et al., DE 19821060 ("Kroczek") in view of Black et al, U.S. Patent No. 6,440,418 ("Black"). According to the Office Action, Kroczek "teaches that antibodies to the 8F4 polypeptide can be used as pharmaceutical compositions to block the interaction of the 8F4 antigen with its receptor in methods of preventing rejection reactions in organ transplants." Although Kroczek does not disclose treatment or prevention of graft versus host reaction, the Office Action asserted that a person of ordinary skill in the art would have arrived at the claimed invention, with a reasonable expectation of success, "because of the teachings of Black et al. that an antibody which inhibit T cell activation and/or T cell-mediated responses, and which are useful in treating transplant rejection, are also useful in treating graft versus host reaction."

Applicants respectfully traverse the rejection in view of the following remarks.

The present application contains working examples demonstrating that *in vivo* administration of an anti-AILIM antibody in an animal model of graft versus host disease significantly suppresses the increase of serum IgG, IgE, and anti-dsDNA antibody titer (indicators of the occurrence of graft versus host reaction) that otherwise occur in the animal model (Example 6 at page 73, line 19, to page 75, line 5). These *in vivo* experiments, performed in an art accepted animal model of graft versus host reaction, establish that an anti-AILIM antibody is effective in the prevention and treatment of graft versus host reaction. Consistent with these experimental findings, claim 18 is directed to a method of preventing or treating graft versus host reaction by administering to a subject a composition containing an antibody or a portion thereof that binds to human AILIM.

To establish a *prima facie* case of obviousness, there must be, *inter alia*, a reasonable expectation of success. MPEP § 2143. The reasonable expectation of success must be in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986). MPEP § 2143.02.

Kroczek describes the production of an antibody directed against the human 8F4 polypeptide and *in vitro* experiments using the anti-8F4 antibody. For example, Kroczek contains working examples demonstrating that an anti-8F4 antibody affects T cell proliferation *in vitro* and apoptosis *in vitro*. However, nothing in Kroczek's experimental findings would have created an expectation that an anti-8F4 antibody would be effective *in vivo* in the treatment of graft versus host reaction. In particular, there is no evidence of record to suggest that a person of ordinary skill in the art would reasonably expect that *any* antibody (such as the anti-8F4 antibody described by Kroczek) that affects T cell proliferation and apoptosis *in vitro* would be effective *in vivo* in treating or preventing graft versus host reaction.

The Office Action cited a passage in Kroczek (at page 12) stating that an anti-8F4 antibody can be used in preventing rejection of organ transplants. Based at least in part upon this passage, the Office Action concluded that an anti-8F4 antibody would also be useful in treating

graft versus host reaction. Although Kroczek's detailed description states that organ transplant rejection can be prevented with an anti-8F4 antibody, there is no experimental description in Kroczek that would have led the skilled person to reasonably expect that an anti-8F4 antibody would in fact be effective in preventing organ transplant rejection, much less be effective in the treatment or prevention of a different disorder such as graft versus host reaction. Kroczek's *in vitro* studies summarized above would have been insufficient to create the requisite expectation of success. In addition to its recitation of prevention of organ transplant rejection, the Kroczek specification also states on page 12 that polypeptides of the invention can be used for the treatment of disorders such as cancers, AIDS, or chronic viral diseases such as HCV or HBV infections (Kroczek at page 12, lines 17-21). Like organ transplant rejection, Kroczek lacks experimental findings that would have led the skilled person to reasonably expect that an anti-8F4 antibody would be effective in the treatment of any of those disorders (or disorders closely related thereto). In view of this deficiency, Kroczek does not create the reasonable expectation of success that would be required to sustain the present obviousness rejection.

Black does not cure the deficiencies of Kroczek. Black describes the characterization of antibodies that bind to gp39, a CD40 ligand expressed on $CD4^+$ T cells. With respect to graft versus host disease, Black cites a study published in the in the prestigious Journal of Clinical Investigation demonstrating that *in vivo* administration of an anti-gp39 antibody "blocked cGVHD-induced serum anti-DNA autoantibodies, IgE production, spontaneous immunoglobulin production in vitro, associated splenomegaly and the ability to transfer disease" (Black at column 5, lines 46-64). In addition, Black refers to the established efficacy of anti-gp39 antibodies in animal models of graft rejection (Black at column 21, lines 60-62, and column 32, lines 50-53). In view of these *in vivo* gp39 studies, the person of ordinary skill in the art having read Black would have reasonably expected that an anti-gp39 antibody can be effectively used to treat or prevent organ transplant rejection and graft versus host reaction. This expectation of success existed for anti-gp39 antibodies because extensive *in vivo* studies related to these two conditions had actually been performed with anti-gp39 antibodies.

Unlike the wealth of *in vivo* data for anti-gp39 antibodies described in Black, there is no experimental data in Kroczek or in any other reference of record that would have led a person of ordinary skill in the art to reasonably expect that anti-8F4 antibodies would be effective in treating or preventing graft versus host reaction. Kroczek's unsupported assertion that such antibodies can be used to prevent organ transplant rejection would not have created this expectation. Nor would Kroczeks' *in vitro* studies related to T cell proliferation and apoptosis. Black's extensive disclosure regarding treatment of graft versus host disease and graft rejection with anti-gp39 antibodies does not compensate for Kroczek's deficiencies with respect to use of anti-8F4 antibodies to treat these conditions. Because the combination of Kroczek and Black do not create a reasonable expectation that an anti-8F4 antibody would be effective in the treatment or prevention of graft versus host reaction, the references do not render obvious the method of claim 18.

In view of the foregoing remarks, applicants respectfully request that the Examiner withdraw the obviousness rejection of claim 18.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is earnestly requested. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 14539-005002.

Respectfully submitted,

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